U.S.S.N. 09/868,664
Filed: May 3, 2001
CLEAN VERSION OF AMENDMENTS PURSUANT TO 37 C.F.R. § 1.121

Clean Version of Amended Claims

Pursuant to 37 C.F.R. § 1.121(c)(1)(ii)

1. (Amended) A drug delivery composition comprising:

a substrate;

a peptide comprising a domain that binds heparin or heparin-like compounds with high affinity,

wherein the peptide is covalently bound to the substrate so that the heparin binding domain is able to bind to heparin or heparin-like compounds;

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heparin or a heparin-like polymer; and

a protein growth factor or a peptide fragment thereof having a domain that binds heparin with low affinity, wherein low affinity is defined as not binding with heparin at a NaCl concentration of between about 25 mM and 140 mM.

3. (Amended) The composition of claim 1 wherein the domain of the growth factor or peptide fragment thereof is further defined as comprising a length of about 8 to 30 amino acid residues comprising at least 2 basic amino acid residues, a ratio of basic to acidic amino acid residues of at least 2, and a ratio of hydrophobic amino acid residues to basic amino acid residues of at least 0.67.

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4. (Amended) The composition of claim 3 wherein the basic amino acid residues are K or R.

5. (Amended) The composition of claim 3 wherein the acidic amino acid residues are further defined as D or E.

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6. (Amended) The composition of claim 3 wherein the hydrophobic amino acid residues are further defined as A, V, F, P, M, I, or L or C when C is involved in a disulfide bond.

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7. (Amended) The composition of claim 1 wherein the growth factor or peptide fragment thereof is selected from the group consisting of neurturin, persephin, IGF-1A, IGF-1β, EGF, NGFβ, NT-3, BDNF, NT-4, TGF-β3, and TGF-β4.

20. (Amended) The composition of claim 65 wherein the substrate comprises fibrin.

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21. (Amended) The composition of claim 65 wherein the substrate comprises a synthetic polymer hydrogel.

24. (Amended) The composition of claim 64 wherein the heparin or heparin-like polymer has a molecular weight between about 3,000 and 10,000,000 Daltons.

25. (Amended) The composition of claim 64 wherein the heparin-like polymer is a polysaccharide having a molecular weight between about 3,000 and 10,000,000 Daltons, and having at least one negative charge per two saccharide rings and no more than one positive charge per ten saccharide rings.

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26. (Amended) The composition of claim 64 wherein the heparin-like polymer is selected from the group consisting of dextran sulfate, chondroitin sulfate, heparin sulfate, fucan, alginate, [or] and a derivative thereof.

27. (Amended) The composition of claim 1 wherein the molar ratio of heparin or heparin-like polymer to growth factor or peptide fragment thereof is at least one.

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57. (Amended) The composition of claim 1 in a vascular graft.

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58. (Amended) The composition of claim 1 in an article for treatment of dermal wounds.

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59. (Amended) The composition of claim 58, wherein the growth factor is TGF-β3.

61. (Amended) The composition of claim 1 in an implantable sterilized composition.

62. (Amended) A method for providing controlled release of a growth factor comprising:

preparing a composition comprising

a substrate,

a peptide comprising a domain that binds heparin or heparin-like compounds, wherein the peptide is covalently bound to the substrate so that the heparin binding domain is able to bind to heparin or heparin-like compounds,

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heparin or a heparin-like polymer, and

a growth factor or a peptide fragment thereof having a domain with low affinity for binding heparin and bound heparin or heparin-like polymer, wherein low affinity is defined as not binding with heparin at a NaCl concentration of between about 25 mM and 140 mM; and

placing the composition on a wound in need thereof.

63. (Amended) The method of claim 62, wherein the growth factor or a peptide fragment thereof is released by dissociation of the growth factor from the heparin or heparin-like polymer.

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64. (New) The composition of Claim 1, wherein the heparin or heparin-like compound is non-covalently attached to the peptide.

65. (New) The composition of Claim 1 wherein the substrate is selected from the group comprising fibrin, collagen and synthetic polymer hydrogels.